Reduction of infarct size

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Editorial Note

Reduction of infarct size: discrepancies between experimental work and clinical application

This issue of the *Journal* contains a convincing example of pharmacological reduction of infarct size after experimental coronary occlusion in rats [1]. Chiariello and coworkers have demonstrated that dilazep, a stimulant of collateral circulation may reduce infarct size by approximately 20% as measured by enzyme depletion in the acute phase and by as much as 40% as measured histologically after 3 weeks.

A naive scientist may ask if patients in coronary wards will now receive dilazep. The clinician knows that the answer is "no". He also knows that it may even take years before a serious clinical trial on the effect of dilazep in patients with acute myocardial infarction will be started. There are seemingly good reasons for this reluctance in acceptance of results obtained in animal studies. Infarct size in patients with acute myocardial infarction shows a large variation. It can be estimated that proof of a 20% reduction of enzyme release after acute myocardial infarction would need a treated and a control group of 100 patients each, which seems impracticable. Another argument concerns the importance of infarct size as a clinical parameter. For instance, in Chiariello's study no significant difference in mortality was observed. However, these arguments are seemingly sound. A large number of studies over the last 10 years have demonstrated the relation between infarct size and mortality or morbidity in patients with acute myocardial infarction and the common sense notion that a small infarction is better than a large one is a proven fact.

In my opinion, the poor follow-up of experimental work by clinical studies is largely a question of trends. One of these present trends has been established by the observation that the border zone between healthy and infarcted myocardium may be quite narrow, suggesting only a small quantity of salvageable tissue [2]. It is surprising to find that direct proof to the contrary, as also given in Chiariello's study, is disregarded in this "border zone" discussion. The importance of trends in this field is also demonstrated by the recent interest in the intracoronary application of streptokinase after acute myocardial infarction. Streptokinase has been used for years and has been proven beneficial in high-risk patients [3]. However, complications such as bleeding and immunological reactions have prevented its widespread use. The dramatic angiographic demonstration of reopening coronary arteries has apparently reduced these objections. (Incidentally, this finding has abolished another trend in denying the role of coronary thrombosis in acute myocardial infarction.) In the case of intracoronary streptokinase there is no experimental evidence that reopening of coronary arteries results in reestablished microcirculation and prevention of irreversible cellular damage. The only two experimental studies in this case

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have, significantly enough, been performed 20 years apart [4,5] and both failed to give quantitative comparisons of infarct size.

The present state of affairs calls for a larger influence of the results of experimental studies on clinical practice. The time between experimental demonstration of a beneficial effect and its clinical application should be reduced, but new clinical treatment should only be introduced after proper experimental evaluation.

References

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